

**Meridian Medical Technologies®, Inc.**  
1945 Craig Road  
St. Louis, MO 63146

July 30, 2017

RECEIVED  
AUG 1 - 2017

BY: .....

Miguel A. Hernández  
Director, Compliance Branch  
US Food and Drug Administration  
8050 Marshall Drive, Suite 205  
Lenexa, KS 66214

RE: Meridian Medical Technologies, Inc. / FEI Number: 1950222  
Quarterly Action Plan Update for 2<sup>nd</sup> Quarter 2017 – Inspection Response Status

Dear Mr. Hernández:

In the April 14, 2017 response to the Food and Drug Administration (“FDA”) Form 483 issued March 24, 2017, Meridian Medical Technologies, Inc. (“MMT”) included a commitment to provide FDA with Quarterly Updates with respect to the 483 response commitments. Also in the response, MMT committed to working with a third party consultant to develop a Compliance Action Plan (“CAP”) which would ensure a holistic response to the 483 observations as well as the broader GMP subsystems implicated by the Observations.

The CAP (exhibit 1) lists several GMP subsystems to be assessed for compliance and improvement opportunities in a prioritized order with a defined timeline. This prioritization was determined using the process stated within the CAP. The CAP was approved on June 30, 2017. Appendix I of the CAP contains the 483 response commitments completed to date and will be updated as future 483 and 3<sup>rd</sup> party assessments commitments CAPA’s are completed.

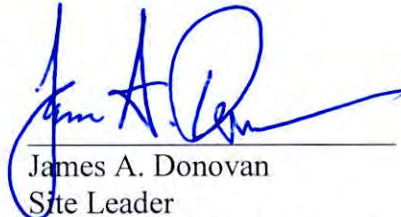
In the 2<sup>nd</sup> Quarter of 2017, all 483/CAP commitment action items that reached their due date were completed on time. The CAP, which includes the most recent approved version of Appendix I is attached as Exhibit I. Appendix I of the CAP was last updated on July 30, 2017. Exhibit 2 is a summary of the CAPA completion status for this overall compliance plan in total, as well as separated out by individual work stream.

Please note that this letter and the corresponding attachments contain confidential information related to MMT's business operations and processes and accordingly are not subject to disclosure under the Freedom of Information Act, 5 USC 552(b)(4) and 21 C.F.R 20.61(a)-(b).

Sincerely,

①

Jeffrey A. Schramer  
Site Quality Operations Leader  
Meridian Medical Technologies, Inc., a Pfizer Company  
1945 Craig Road  
St. Louis, MO 63146  
(269) 207-7624



James A. Donovan  
Site Leader  
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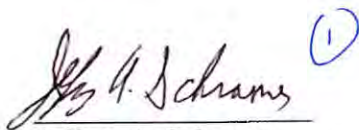
cc: Cheryl Bigham  
District Director, Kansas City District Office

① See attached additional signature page for Jeff Schramer  
wet signature signed on 30 Jul 2017 onto photocopied James  
Donovan signature page (which was also signed on 30 Jul 2017.  
J.A. Schramer 31 Jul 2017

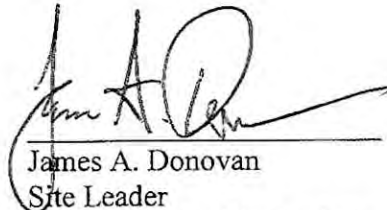
In the 2<sup>nd</sup> Quarter of 2017, all 483/CAP commitment action items that reached their due date were completed on time. The CAP, which includes the most recent approved version of Appendix I is attached as Exhibit I. Appendix I of the CAP was last updated on July 30, 2017. Exhibit 2 is a summary of the CAPA completion status for this overall compliance plan in total, as well as separated out by individual work stream.

Please note that this letter and the corresponding attachments contain confidential information related to MMT's business operations and processes and accordingly are not subject to disclosure under the Freedom of Information Act, 5 USC 552(b)(4) and 21 C.F.R 20.61(a)-(b).

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cc: Cheryl Bigham  
District Director, Kansas City District Office

① This is additional signature page for wet signature of Jeff Schramer. J.A. Schram 31 Jul 2017

Exhibit 1. Compliance Action Plan (CAP) – (approved 30Jun2017) with Most Current CAP  
Appendix I (last updated July 30, 2017)



## Compliance Action Plan (CAP)

for:

Meridian Medical Technologies, Inc.  
St. Louis, MO

June 29, 2017

Prepared By / Date:

*Jeff A. Schramer 29 Jun 2017*

Jeffrey A. Schramer  
Site Quality Leader, MMT

Approved By / Date:

*Tom Handel 29 JUNE 2017*

Tom Handel  
President and General Manager, MMT

Approved By / Date:

*(1)*

Kevin Jenkins  
Vice President of Quality Excellence, Pfizer Corporation

① See signed cover page of emailed scan. Scan signed by K. Jenkins on 30 Jun 2017. J.A. Schramer 26 Jul 2017



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## Compliance Action Plan (CAP)

for

Meridian Medical Technologies, Inc.  
St. Louis, MO

June 29, 2017

Prepared By / Date:

Jeffrey A. Schramm 27 Jun 2017  
Jeffrey A. Schramm  
Site Quality Leader, MMT

Approved By / Date:

Tom Handel 29 JUNE 2017  
Tom Handel  
President and General Manager, MMT

Approved By / Date:

Kevin Jenkins 30 June 2017  
Kevin Jenkins  
Vice President of Quality Excellence, Pfizer Corporation

## **Index**

1. Introduction
  2. Purpose
  3. Governance and Oversight
  4. Approach and Methodology
  5. CAP Scope
  6. Project Overview
  7. Third Party Audit Details
  8. Project Deliverables
  9. Communication
  10. Criteria for Success
- APPENDIX I- CAPA Tracking (Updated (b) (4) )



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## 1. INTRODUCTION

Meridian Medical Technologies, Inc., a Pfizer Company (hereafter MMT) located at St Louis, MO, was inspected by the U.S. Food and Drug Administration (FDA) from February 20 through March 24, 2017. At the conclusion of the Agency's inspection on March 24, 2017, MMT received a Form 483 with 14 multi-part observations relating to the manufacture of the firm's auto-injector combination products.

MMT submitted a written response to the Form 483 on April 14, 2017. Within the response was a commitment to engage a third party consultant that specializes in Quality System Remediation. To that end, (b) (4) was retained by MMT as the identified 3<sup>rd</sup> party in May 2017. Specifically, (b) (4) involvement was to review and provide input to this document, to conduct in-depth audits of the three (3) priority topics listed directly below in the next paragraph, and to identify the topics/areas listed under Section 5 that are in need of a rigorous audit, in order to establish the level of compliance.

One of the deliverables within the 483 Response, was for MMT to create a Compliance Action Plan (CAP). It was communicated within our 483 response that the CAP would focus on three key areas for assessment by the 3<sup>rd</sup> party, which would then result in corresponding improvement commitments by MMT. The following systems communicated to be further assessed by a 3<sup>rd</sup> party are:

- o Design Controls
- o Complaint Investigations
- o AQLs (Sampling Plans)

Furthermore, the 483 Response stated the CAP would include any new commitments that arise from gap assessments/reviews performed as part of the 483 response commitments, as well as any additional quality systems requested for evaluation by a 3<sup>rd</sup> party consultant.

## 2. PURPOSE

The CAP is intended to document corrective and preventive actions arising from assessment work described above, in addition to the commitments previously provided in MMT's original April 14, 2017 483 Response. This CAP supplements the Form 483 response and provides assurance that a comprehensive, holistic approach is being taken by MMT. The CAP will also be utilized to document corrective and preventative action effectiveness checks (which will be conducted by a 3<sup>rd</sup> party) for all commitments within the CAP.

The in depth 3<sup>rd</sup> party assessments of existing systems and CAPA effectiveness verification work will follow completion of the initial version of this CAP. CAP Appendix I will be updated on (b) (4) basis to provide tracking information to the

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compliance initiatives stated within the CAP and each update will be approved by management.

### 3. GOVERNANCE AND OVERSIGHT

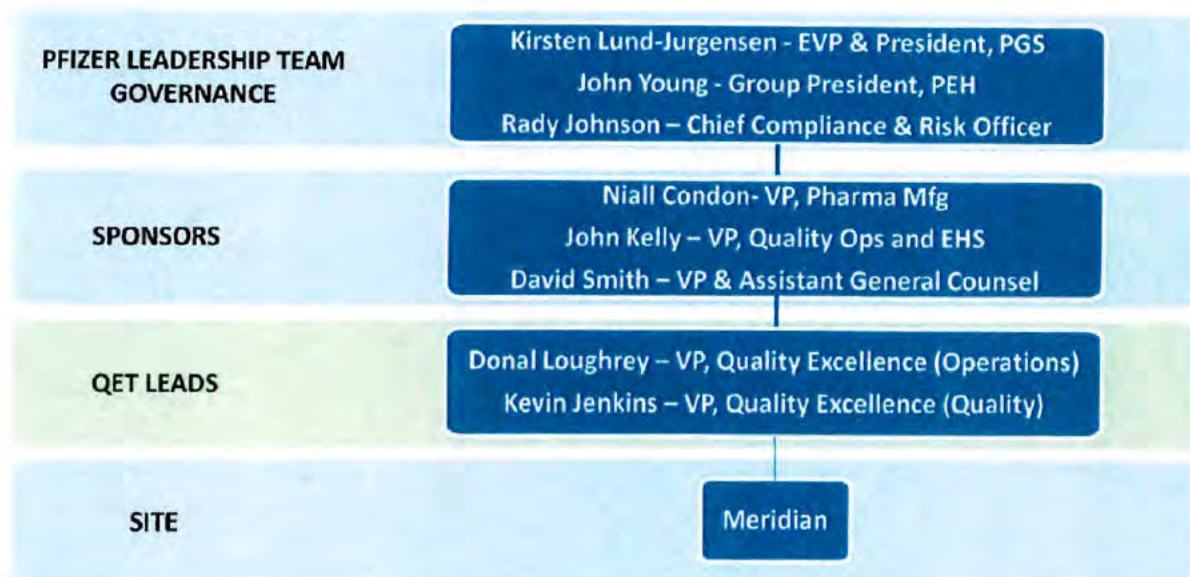
In order to provide focused resources for manufacturing sites undergoing remediation, Pfizer established a Quality Excellence Team (QET) to provide focus and support on improvement at sites undergoing remediation in May 2017. The QET is co-led by Operations and Quality, with dual reporting to the VP Pharmaceutical Manufacturing Operations and the VP Quality Operations and Environmental Health & Safety and accountability to Pfizer's Leadership Team Governance as described below.

The objective of the QET is to deliver a focused and aligned approach to development and execution of quality improvement activities at selected network sites in order to achieve/maintain Voluntary Action Indicated (VAI) status. The team's responsibilities include the following:

- Ensuring comprehensive quality improvement plans for each site in scope are in place and incorporate actions and recommendations from regulatory inspections and internal/external assessments
- Providing above site project management, as well as frequent updates to sponsors
- Ensuring projects are prioritized and resourced appropriately and programs/training are developed as needed
- Accelerating key projects and driving overall timelines, ensuring regulatory commitments are made
- And ensuring consistency for specific improvements applicable across multiple sites.

The integration of the CAP deliverables into the QET Oversight and Governance process are further described in the Communication section of this document.

Below is the governance structure of the QET:



#### 4. APPROACH AND METHODOLOGY

Development of this CAP included (b) (4) review of the Form 483 observations, MMT's responses, physical inspection/tours of buildings and facilities, performing reviews of records and procedures, and conducting interviews with MMT management and key staff personnel.

#### 5. CAP SCOPE AND TIMING

As described in the FDA response commitment letter, MMT previously identified three key areas for improvement that will be a primary focus of the 3<sup>rd</sup> party assessments required for the CAP, namely:

- Design Controls
- Complaint Investigations
- AQLs (Sampling Plans)

Additionally, other areas / topics for evaluation were identified by either MMT or (b) (4) through staff interviews, document reviews and facility tours that were conducted by (b) (4) during the weeks of May 15, May 22, and June 5, 2017. A tiered risk-ranking was performed for all the topics identified. Risk was predicated on potential impact to patient safety, product quality, pre-existing internal assessments/improvement plans, and/or regulatory compliance. Other factors

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considered with respect to risk were: whether the issues identified by FDA and MMT's proposed corrective actions appeared to have a comprehensive approach toward resolution as described in the MMT 483 response (per (b) (4) evaluation of MMT's 483 response), whether the issues within the FDA 483 were one-off occurrences vs. systemic cause; or other factors that suggested a comprehensive evaluation was warranted. The priorities for the comprehensive evaluations to be conducted by the 3<sup>rd</sup> party are below, and separated into two phases. (b) (4)

(b) (4) Below are the quality systems and timelines expected for PHASE I and PHASE II:

**PHASE I (PARAXEL Assessments of the PHASE I topics below are expected to be completed by July 15, 2017, and the corresponding MMT CAPAs to be identified by July 30, 2017)**

(b) (4)

**PHASE II (3<sup>rd</sup> Party Consultant Assessments to be completed by October 1, 2017, and the corresponding MMT CAPAs to be identified by October 31, 2017)**

(b) (4)

## 6. PROJECT OVERVIEW

The objectives of this CAP will be achieved by completion of the following key steps:

(b) (4)

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## 7. THIRD PARTY AUDIT DETAILS

A more detailed description of the comprehensive 3<sup>rd</sup> party evaluations described within Section 5 Phase I and II is as follows:

(b) (4)

## 8. CORRECTIVE AND PREVENTATIVE ACTIONS

(b) (4)



(b) (4)

#### 9. COMMUNICATION

A Steering Committee comprised of leadership with executive responsibility for MMT and QET Leads will meet (b) (4) to discuss progress on the Compliance Action Plan.

Standing agenda for the (b) (4) meetings are to include:

- Action Items
- CAPA Commitment Dashboard
- (b) (4) Snapshot (recently completed activity and look ahead to the coming actions)
- Staffing Update
- Discussion Items
- Any specific commitment detail that needs Governance visibility/alignment
- Routine Quality Performance - Investigation Status

The CAP APPENDIX I will be updated on a (b) (4) The CAP and the newly updated APPENDIX I will be provided to the FDA within one month following the (b) (4) update of APPENDIX I, until such time that all 483 Response and CAP related CAPA are completed along with successful effectiveness checks.

#### 10. CRITERIA FOR SUCCESS:

Criteria for determining project success include, but are not limited to, the following:

(b) (4)



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**APPENDIX I**  
**Compliance Action Plan Related CAPA Status**  
**(Version 2.0 Updated Date- 30 July 2017)**

**APPENDIX I Update Prepared By / Date:**

Nicole Typaldos 30 Jul 2017  
**Nicole Typaldos**  
**Quality Systems Manager, MMT**

**APPENDIX I Approval By / Date:**

Jeff A. Schramer 30 Jul 2017  
**Jeffrey A. Schramer**  
**Site Quality Leader, MMT**

**Table I**

**Third Party Assessment Tracking**

**(b) (4)**

**Table II FDA 483 Related Corrective and Preventative Action Tracking, by order of Observation and Due Date**

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	Cover Letter	MMT will engage SME's within the Pfizer / Meridian / Industry network and experienced independent consultants with significant experience with medical device quality systems to develop a Compliance Action Plan (CAP) that will identify corrective and preventative actions that will enhance our systems and processes. The CAP will focus on three primary areas for improvement, as identified in the observations and our own internal discussions: Design controls (including DHF) Complaint Investigations Acceptable Quality Limits (AQL) DRAFT	15-Jun-17	15-Jun-17	Quality Systems		
FDA Inspection	Cover Letter	Submit updates to FDA on a quarterly basis, with the first update to be submitted by July 30, 2017 (for the three month period ending June 30, 2017). First Update will include a copy of our CAP.	30-Jul-17		Quality Systems		
FDA Inspection	1, 4, 6, 8	<p>Update the standard sampling plan for EpiPen finished good functionality test to (b) (4) units (b) (4) (b) (4) AQL from (b) (4) to (b) (4)</p> <p>The current AQL of (b) (4) sampling plan (for critical defects) will be modified to yield a (b) (4) AQL of (b) (4) final product functionality testing.</p> <p>The current AQL of (b) (4) sampling plan (for critical defects) will be modified to yield a (b) (4) AQL of (b) (4) for product release testing. (See Response 6A table 4)</p> <p>The current AQL of (b) (4) sampling plan (for critical defects) will be modified to yield a (b) (4) AQL of (b) (4) for product release testing. (See Response 6A table 4)</p> <p>(b) (4) AQL applied for release testing will be instituted</p> <p>For those essential functional attributes as design inputs and outputs are confirmed critical through risk assessment process, (b) (4)</p>	30-Apr-17	28-Apr-17	Laboratory		

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Page 2 of 24

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
		specification with (b) (4) AQL for determination of sample size will be applied for release testing reflecting system level reliability.					
FDA Inspection	1, 13	SOP-QLA-MQA-00720 to be updated to assure consistent application across lots in the scope of an investigation when additional testing is performed to evaluate potential quality impact SOP-QLA-MQA-00720 will be revised to require that all on-going preventative actions that address root cause are included in an investigation report SOP-QLA-MQA-00720 will be revised to require that deviation investigators implement the use of (b) (4) to identify when the item or event being investigated differs from historical process trend as an aid in the investigation process SOP-QLA-MQA-00720 will be revised to include an instruction that the potential impact of reprocessing or atypical environmental conditions, such as (b) (4), be considered during relevant investigations	31-May-17	30-May-17	Quality Systems		
FDA Inspection	1	Update SOP-QLA-MQA-00004 to ensure that formal notification to management occurs for any OOS result, whether it be for a finished product, in-process sample, or incoming component	31-May-17	30-May-17	Quality Systems		
FDA Inspection	2	SOP-MAN-INS-00029 will be updated to add specific requirements for the (b) (4) for all product lines	31-May-17	19-May-17	P&I		
FDA Inspection	2, 14	New Job Aid to be created which includes (b) (4) and further details for the steps performed during the (b) (4) New OJT training document will be developed and implemented for all colleagues that perform (b) (4). The new OJT will require review of the job aid, review of SOP-PRO-CLP-00005, and hands on training (New Job Aid to be created which includes (b) (4) and further details for the steps performed during the (b) (4)	7-Jun-17	2-Jun-17	Aseptic Operations		
FDA Inspection	2	MVI performance improvement: (b) (4)	30-Jun-17	23-Jun-17	P&I		

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Page 3 of 24

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	2	AQL sampling will be adjusted so that results of the sampling are (b) (4) (b) (4)	31-Jul-17	28-Jul-17	P&I		
FDA Inspection	2	MVI performance improvement: (b) (4) Any improvement opportunities will be incorporated into a process continuous improvement plan	31-Aug-17		P&I		
FDA Inspection	2	(b) (4)	30-Nov-17		P&I		
FDA Inspection	3	Statistical Analysis with a (b) (4) (b) (4) Based on the analysis, statistically based lot trend alert limits will be identified for complaint sub-classes.	15-May-17	15-May-17	Complaints		
FDA Inspection	3, 13	SOP-QLC-QLE-00702 will be revised to clarify that site personnel can and should take action to address any combination of complaints, no matter the number, that appears to signal a trend or issue and to establish the following expectations with respect to alert limits: - statistically based alert limits for the number of complaints of a similar nature for the same lot for all products and all complaint sub-classes - a requirement that lot trend alert limits are based on statistical analysis of historical complaint data - a requirement that the statistically based lot trend alert limits be reviewed at least annually SOP-QLC-QLE-00702 will be revised to include an instruction that the potential impact of reprocessing or atypical environmental conditions, such as (b) (4) be considered during relevant investigations	31-May-17	31-May-17	Complaints		
FDA Inspection	3	Pfizer corporate procedure GPB-QS1073 will be updated to clarify the purpose of the expedited complaint process. As part of the update, all complaint classifications associated with devices and combination products will be evaluated to ensure alignment to the requirements of the specific regulatory notifications described above. In addition, all complaint classifications associated with the products manufactured at MMT will also	30-Jun-17	30-Jun-17	Complaints		

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Page 4 of 24

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
		be evaluated to ensure that any product specific exceptions regarding prioritization are included in the update to GPB-QS1073.					
FDA Inspection	3	SOP-QLC-QLE-00702 will be updated to reflect the clarifications in GPB-QS1073 regarding the purpose for expediting complaints	15-Jul-17	15-Jul-17	Complaints		
FDA Inspection	3	Risk Assessment will be performed including Safety/Medical/Clinical, to document the rationale for the ranges of the essential performance inputs and their criticality/severity based on the emergency, life-saving intended use of the product. The risk assessment will also establish acceptable mean complaint rates and will be reviewed at a minimum of annually as part of the Annual Product Review	31-Jul-17	28-Jul-17	Complaints		
FDA Inspection	3	Engaging experienced independent consultants with significant experience with medical device quality systems to conduct an assessment of the MMT quality systems, including Complaint Management. Assessment	31-Aug-17		Quality Systems		
FDA Inspection	3	Creation of Action Plan with timeframe for corrective actions (from consultant assessment of Complaints)	30-Sep-17		Complaints		
FDA Inspection	4	New procedure to conduct (b) (4) has been drafted and will be approved. (SOP-QLA-GEN-11104)	15-May-17	15-May-17	Operational Excellence		
FDA Inspection	4	A detailed roll-out plan for (b) (4) will be approved by Manufacturing and Quality. The (b) (4) to be conducted under the scope of the new procedure will be for the filling equipment for (b) (4) (b) (4)	30-May-17	30-May-17	Operational Excellence		

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	4	Procedure will be developed by Operational Excellence, Manufacturing, and Quality to require routine in-process trending for ATNAA and EpiPen and to assess performance variability A new procedure will be developed by MMT to require routine in-process data trending of critical parameters to assess performance variability for ATNAA and EpiPen	30-Jun-17	23-Jun-17	Operational Excellence		
FDA Inspection	4	Risk assessment, including representatives from the Safety/Medical/Clinical groups to document essential attributes for intended use and their criticality.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	4	In-process trending at the site will be in place for identified critical processing areas. A review of these trend reports will be incorporated into periodic reviews in the APRR.	30-Aug-17		Quality Systems		
FDA Inspection	4	In-process trending at the site will be in place for identified critical processing areas. A review of these trend reports will be incorporated into periodic reviews at SQRT.	30-Aug-17		Quality Systems		
FDA Inspection	4	Updates to the Process Maps are also being developed for current the products currently being manufactured at the site, ATNAA, to identify process input variables that can be further evaluated to enhance process capability. (ATNAA Filling)	31-Aug-17		Operational Excellence		
FDA Inspection	4	(b) (4)	31-Aug-17		Operational Excellence		
FDA Inspection	4	Updates to the Process Maps are also being developed for current the products currently being manufactured at the site, ATNAA, to identify process input variables that can be further evaluated to enhance process capability. (ATNAA P&I)	31-Aug-17		Operational Excellence		
FDA Inspection	4	For those essential characteristics that are confirmed in the risk assessment and defined as critical in Table 2 of Response 6A, there will be a plan implemented to conduct testing based on system level reliability.	31-Aug-17		Design Controls		

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	4	(b) (4) batch records	30-Sep-17		P&I		
FDA Inspection	4	(b) (4) batch records	30-Sep-17		P&I		
FDA Inspection	4	Trend reporting, including (b) (4) will be incorporated into periodic reviews at Site Quality Review Team (SQRT) meetings for continuous improvement	31-Oct-17		Quality Systems		
FDA Inspection	4	Trend reporting, including (b) (4) will be incorporated in the Annual Product Records Review (APRR) for continuous improvement	31-Oct-17		Quality Systems		
FDA Inspection	4	As an outcome of the capability studies, Six-Sigma projects will be employed to reduce variability where improvement areas are identified. Results from the capability studies will be incorporated into periodic reviews of Site Quality Review Team.	28-Feb-18		Quality Systems		
FDA Inspection	4	As an outcome of the capability studies, Six-Sigma projects will be employed to reduce variability where improvement areas are identified. Results from the capability studies will be incorporated in the Annual Product Record Review (APRR).	28-Feb-18		Quality Systems		
FDA Inspection	5	Complaint trend reports will be based on (b) (4) (b) (4) These additional site trend reports will be presented in SQRT and incorporated in the APRRs to identify any corrective actions needed. A plan for implementing these additional reports (data collection method, procedures, etc.) will be developed and implemented thereafter.	15-Jul-17	14-Jul-17	Complaints		

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6	Evaluate SOP-DVL-PRT-00002 procedure for potential updates to include the development of a system level reliability and to ensure linkage to the design outputs. The procedure will be applied to (b) (4) products. The procedure will require the Design Input document, PRD/TRD, to include cross reference to the risk assessment and documentation supporting the individual design inputs. Training methodology using human performance tools will be developed to assure adherence with the procedure	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6, 7, 8	Risk Management file will be updated with a risk assessment performed by a CFT including representatives from Safety/Medical/Clinical groups, to document essential attributes and their criticality and rationale for design inputs. Risk Management file will be updated with a risk assessment including representatives from Safety/Medical/Clinical to document the rationale for the ranges of the essential performance inputs and their criticality/severity based on the emergency, life-saving intended use of the product. The risk management file will be updated with a risk assessment including review by representatives from Safety/Medical/Clinical to document the rationale for the ranges of the essential performance inputs and their criticality based on the emergency, life-saving intended use of the product. Risk Management file will be updated with a risk assessment (states CFT (S/M/C) will be completed JUL2017) The risk management file will be updated with a risk assessment.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	MMT will evaluate potential foreseeable sequential preconditioning of auto-injectors to include in reliability testing. System level reliability risk assessment will be completed	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	MMT will evaluate its design input procedures for potential updates to include development of system level reliability.	31-Jul-17	28-Jul-17	Design Controls		

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6	The design inputs document will be updated for consistency between the product requirements section and the technical requirements section.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	Risk Management file will be updated with a risk assessment performed by a cross-functional team, including Safety/Medical, to confirm essential attributes and their criticality based on severity of harm and intended use of the combination product. The PRD/TRD design inputs document will be reviewed to ensure completeness and that the inputs are written in a non-conflicting or ambiguous way.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	PRD/TRD 16-001 rev 1, design inputs document, will be updated to include the system level reliability specification of (b) (4)	31-Aug-17		Design Controls		
FDA Inspection	6, 7	<p>The PRD/TRD design input document will be updated to include cross reference to the risk assessment and documentation supporting the risk assessment conclusions.</p> <p>PRD/TRD design inputs document will be reviewed to ensure completeness and that the inputs are not written in a conflicting or ambiguous manner.</p> <p>MMT will update the PRD/TRD to trace the requirements to appropriate justifications and risk assessment. The design inputs document format will be revised to eliminate ambiguity between "Must" and "Want" design inputs. The "Wants" requirements of a PRD/TRD document will be removed from the document prior to finalizing design outputs such that design outputs can be traced directly to design in/out requirements.</p> <p>PRD/TRD 16-001 Rev I, injection through clothing is a requirement included as part of the use specification. This will be added to the Technical Requirement of the PRD/TRD design input document</p> <p>MMT will review the PRD/TRD, design inputs document, to ensure completeness and that the inputs and outputs are not written in a conflicting or ambiguous manner.</p>	31-Aug-17		Design Controls		

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6	CFT (S/M/C) risk assessment completion. Risk control within the supply chain control plan will be evaluated to verify it supports the recommended system level reliability	31-Dec-17		Design Controls		
FDA Inspection	6, 7	<p>For those essential characteristics that are confirmed as critical in Table 2 of Response 6A, or modified per the safety/medical risk assessment, (b) (4) specification based on acceptable use for all EpiPen products including the proposed (b) (4)</p> <p>For those essential attributes that are confirmed critical through the risk assessment process, a (b) (4) specification, based on acceptable use</p> <p>For those essential functional attributes as described in Table 2, part 6A a (b) (4) specification based on User/Patient needs will be reassessed to determine an appropriate AQL or quality standard that sets a test sample size commensurate with demonstrating system level reliability.</p> <p>For those essential functional attributes as described in Table 2, part 6A a (b) (4) specification based on User/Patient needs will be reassessed to determine an appropriate AQL or quality standard that sets a test sample size commensurate with demonstrating system level reliability. These values will be applied to all relevant documents and the necessary updates will be made.</p>	31-Dec-17		Design Controls		
FDA Inspection	7, 8	<p>MMT will take the preventative action to evaluate SOP-DVL-PRT-00003 for linking design outputs to the design input requirements and the procedure will be updated as required to include a cross reference of design output conformance to design inputs. Training methodology using human performance tools will be used to assure adherence with the updated procedure.</p> <p>Evaluate SOP-DVL-PRT-00003 for linking design outputs to the design input requirements and the procedure will be updated to include evaluations of design output conformance to design inputs. Training methodology using human performance tools will be used to assure adherence with the procedure</p>	31-Jul-17	28-Jul-17	Design Controls		

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Page 10 of 24

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	7	Design outputs will be reviewed to ensure completeness	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	7, 8	<p>As part of our corrective action the design inputs requirements of PRD/TRD 16-001 Rev 1 will be updated to include the system level reliability requirement of (b) (4)% for essential performance requirements and reasonably foreseeable sequential pre-conditioning. This will be documented as a design output, in the engineering drawings: (b) (4)</p> <p>As part of our corrective action the design inputs requirements of PRD/TRD 16-001 Rev 1 will be updated to include the system level reliability requirement of (b) (4)% for essential performance requirements and reasonably foreseeable sequential pre-conditioning. This will be documented as a design output, in the engineering drawings: (b) (4) Reliability will then be defined in the design output and used to determine design verification requirements.</p>	31-Aug-17		Design Controls		
FDA Inspection	8	Evaluate the design verification and validation procedure SOP-DVL-PRT-00004 for linking design verification requirements to the design input and output requirements. The procedure will be updated and training methodology using human performance tools will be used to assure adherence with the procedure	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	Evaluate the design control procedures for needed updates to ensure linkage of design verification requirements to the design input and outputs. Training methodology using human performance tools will be used to assure adherence with the procedure.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	Design Control Procedures will be updated to require evaluation of foreseeable sequential conditioning	31-Jul-17	28-Jul-17	Design Controls		

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Page 11 of 24

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	8	Design inputs and outputs will be reviewed to ensure completeness.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	MMT will develop through the risk assessment process the foreseeable sequence of conditioning requirements for design verification and commercial process validation functional testing to be included as a component of the design verification and design validation plans. PRD/TRD 16-001 Rev 1 will be updated to include requirements for foreseeable sequential testing.	31-Aug-17		Design Controls		
FDA Inspection	8	Execute a study with full functional system level reliability testing including sequential foreseeable preconditioning of auto-injectors, if required, using (b) (4) require functional system level reliability testing of the auto-injector device at end of product expiry. (b) (4) stability for future submission lots. For submissions (b) (4) may be included	30-Sep-17		Design Controls		
FDA Inspection	8	Execute a design verification study with full functional system level reliability testing including sequential foreseeable preconditioning of auto-injectors, if required (b) (4) (b) (4)	31-Dec-17		Design Controls		
FDA Inspection	9	Basic unit dFMEA will be approved.	31-May-17	25-May-17	Design Controls		
FDA Inspection	9	Basic unit dFMEA will be (b) (4) (b) (4)	31-Aug-17		Design Controls		



Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	9	dfMEA risk assessment will be incorporated into the plant quality systems including QTS, Complaints, Change Control and for risk management.	15-Nov-17		Quality Systems		
FDA Inspection	9	The dfMEA reference (b) (4) will be reviewed at a minimum of annually as part of the APRR	28-Feb-18		Quality Systems		
FDA Inspection	10	A new procedure to address preventive maintenance for the (b) (4) the auto-injectors (SOP-QLC-SQC-11108)	30-Apr-17	28-Apr-17	Laboratory		
FDA Inspection	10	SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394 will be revised by April 30, 2017 to (b) (4) SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394, will be (b) (4) performance of the test	30-Apr-17	28-Apr-17	Laboratory		
FDA Inspection	10	Preventative maintenance procedures for all other equipment in the lab will be confirmed	30-Apr-17	28-Apr-17	Laboratory		
FDA Inspection	10	A (b) (4) (b) (4) Action items will be established if any statistical differences are identified.	15-May-17	15-May-17	Operational Excellence		

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Page 13 of 24

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	10	A FMEA will be completed to identify and prioritize potential failure modes in the functional lot release test procedures and testing process. A plan to implement mitigating actions for any failure modes with unacceptable risk priority numbers.	15-Jun-17	15-Jun-17	Laboratory		
FDA Inspection	10	A process has been developed for the (b) (4) Administrators to prompt and follow up with managers to create/modify curricula for new employees, new contingent staff or staff with job assignment changes. This process is already in place, but will be formally defined in a new (b) (4) SOP.	30-Jun-17	30-Jun-17	Quality Systems		
FDA Inspection	10	New (b) (4)	15-Jul-17	15-Jul-17	Laboratory		
FDA Inspection	10	SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394, will be enhanced to provide specific instructions for the (b) (4) [ (b) (4) will be added the SOPs to ensure (b) (4) The additional detail will describe what types of (b) (4)	31-Jul-17		Laboratory		
FDA Inspection	10	MMT curricula and curricula assignments for all colleagues will be reviewed by the responsible area manager or their designee to ensure assignments are correct and complete. This will be facilitated by Training Systems and area training staff and formally documented according to SOP-TRN-GEN-00044, curricula reviews will be completed (b) (4) thereafter.	31-Aug-17		Quality Systems		

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Page 14 of 24

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	10	MMT will evaluate the potential to (b) (4) This would (b) (4)	30-Sep-17		Laboratory		
FDA Inspection	11	SOP-LAB-MIC-00416 will be revised to also include this same holistic review of all lots that could be in scope of a sterility test failure, in accordance with SOP-QLA-MQA-00720	30-Jun-17	8-Jun-17	Laboratory		
FDA Inspection	12	Awareness training will be performed to (b) (4) (b) (4) This activity will be covered by all (b) (4) and will take place prior to (b) (4)	30-Apr-17	26-Apr-17	Aseptic Operations		
FDA Inspection	12	(b) (4) (b) (4) These tools will better facilitate the (b) (4)	15-Jun-17	8-Jun-17	Aseptic Operations		
FDA Inspection	12	(b) (4) (b) (4). The (b) (4) in this area of the filling process will enhance (b) (4) and reduce potential for human intervention during the (b) (4) (b) (4) project's comprehensive validation.	15-Jun-17	14-Jun-17	Aseptic Operations		

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	12	(b) (4) will be enhanced at the mid-June (b) (4) implementation. Applicable site personnel will train on this documentation update and the action will be added to the aseptic training program	15-Jun-17	13-Jun-17	Aseptic Operations		
FDA Inspection	12	Methods for (b) (4) by the corporate Microbial and Aseptic Support group by mid-June 2017	15-Jun-17	15-Jun-17	Laboratory		
FDA Inspection	12	An (b) (4) will be developed by July 1, 2017 as needed based on the findings of the evaluation	1-Jul-17	30-Jun-17	Aseptic Operations		
FDA Inspection	12	A (b) (4) on the (b) (4) Th (b) (4) will enhance (b) (4) and reduce potential for human intervention during the (b) (4) (b) (4) project's comprehensive validation.	20-Jul-17	19-Jul-17	Validation		
FDA Inspection	12	New production procedure will be created to include examples in which (b) (4)	20-Sep-17		Aseptic Operations		
FDA Inspection	12	SOP-QLA-VAL-00020 will be revised to require each (b) (4) media fill to produce a (b) (4) for a required (b) (4)	31-Oct-17		Validation		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	12	MMT will engage SME's within Industry network with expertise in the design of (b) (4) to evaluate whether (b) (4) to reduce the risk of contamination during intervention (b) (4) and all other interventions performed on the (b) (4).	31-Dec-17		Aseptic Operations		
FDA Inspection	12	Based on the conclusions of the evaluation, an action plan will be developed by January 31, 2018 to implement equipment modifications or other recommendations made by the expert.	31-Jan-18		Aseptic Operations		
FDA Inspection	13	Current instructions on (b) (4) will be clarified to (b) (4) e.g. (b) (4) SOP-MAN-INS-10154, RM-MAN-INS-10153, RM-MAN-INS-10152 and RM-MAN-PKG-10159 will be updated to include these instructions	15-May-17	15-May-17	P&I		
FDA Inspection	13	A (b) (4) will be performed. The (b) (4) (b) (4) During the (b) (4) will represent worse case conditions. Results from the (b) (4) will be compared to determine if any additional (b) (4) should be implemented	30-Jun-17	29-Jun-17	Validation		
FDA Inspection	13	SOP-QLA-GEN-00802 will be revised to define requirements and provide examples for when to perform change effectiveness checks and risk assessments, specifically, for (b) (4) (b) (4)	31-Aug-17	30-May-17	Validation		

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Page 17 of 24

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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	13	Full process validation from formulation through labeling of the assembled units will be completed (to (b) (4) of the complete manufacturing process) – EpiPen	15-Dec-17		Validation		
FDA Inspection	13	Full process validation from formulation through labeling of the assembled units will be completed (to (b) (4) of the complete manufacturing process) - ATNAA/DuoDote	29-Jun-18		Validation		
FDA Inspection	n/a verbal	Update the MMT complaint SOP to (b) (4) complaint type based upon a review of historical complaint rates. Implement similar complaint (b) (4) complaint types.	31-May-17	31-May-17	Complaints		
FDA Inspection	n/a verbal	Update Annual Product Records Review procedure SOP-QLA-MQA-00710 to include sections on: 1. Trending, tracking and (b) (4) for product defects 2. (b) (4) Analysis	31-May-17	31-May-17	Quality Systems		
FDA Inspection	n/a verbal	Change acceptance criteria in the final product release batch records to require (b) (4) average specification for (b) (4)	31-May-17	25-May-17	Laboratory		
FDA Inspection	n/a verbal	Automated vision systems for 100% inspection of the power pak (b) (4) (b) (4) (b) (4)	20-Sep-17		Quality Systems		

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**Table III** CAP Related Corrective and Preventative Action Tracking as a Resulting from work completed under 483 commitments (by order of Due Date)

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	(b) (4)						
CAP							
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(b) (4)

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CAP

(b) (4)

**Table IV** CAP Related Corrective and Preventative Action Tracking as a Result of 3<sup>rd</sup> Party (b) (4) (by order of Due Date)

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
<b>Compliance Action Plan – Design Controls Assessment &amp; Statistical Methods Assessment</b>						
CAP	(b) (4)					
CAP						
CAP						
CAP						
CAP						
CAP						
CAP						



CAP	<div>(b) (4)</div>
CAP	
CAP	
CAP	
CAP	
CAP	
CAP	
CAP	
CAP	
CAP	
CAP	
CAP	
Compliance Action Plan – Product Complaint System Assessment	



CAP	(b) (4)
CAP	
CAP	
Compliance Action Plan – Investigation Systems Assessment	
CAP	(b) (4)
CAP	
CAP	
CAP	
CAP	

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Exhibit 2. Compliance Action Plan (CAP) dashboard (last updated July 30, 2017)

(b) (4)